REVIEWS.

ART. XIII.—*Diseases of the Liver.*

1. *On the Bile, Jaundice, and Bilious Diseases.* By J. WICKHAM LEGG, F.R.C.P. London; Assistant Physician to St. Bartholomew's Hospital, and Lecturer on Pathological Anatomy in the Medical School. 8vo. pp. 719. New York: D. Appleton & Co., 1880.
2. *Diseases of the Liver and Portal Vein, being Volume IX. of Ziemssen's Cyclopædia.* New York: William Wood & Co., 1880.
3. *Clinical Lectures on Diseases of the Liver, Jaundice, and Abdominal Dropsy.* By CHARLES MURCHISON, M.D., LL.D., F.R.S. Second edition. New York: William Wood & Co., 1877.
4. *A Clinical Treatise on Diseases of the Liver.* By Dr. THEOD. FRIED. FRERICHS. Two volumes. The New Sydenham Society, London, 1860.

A COMPARISON of the most recent with the older works on the diseases of the liver, placed at the head of this article, will indicate the progress made in our knowledge, not only of the pathological states, but, also, of the functions, of this important organ. If we may interpret Dr. Legg's rather satirical expressions literally, it would not be an anachronism to place amongst these modern authorities the works of Galen, whose knowledge of the biliary functions seems to have been little inferior to our own. Says Dr. Legg, "those who come after us may judge whether the nineteenth century has made any real progress in this matter, compared with the age of Galen." Notwithstanding the temptation to which we are thus exposed, it would be quite impracticable to embrace the works of Galen in the scope of our inquiry. The great treatise of Frerichs, the appearance of which was, in a certain sense, the beginning of a new era in the clinical study of hepatic affections, is a convenient point from which to undertake a review of the subject. It would, indeed, be a labour of supererogation, at this period, to set before our readers an account of this monumental work. The position which we have assigned it, in the course of the historical development of the subject, will probably not be questioned. Murchison's volume, a strictly clinical treatise, is an obvious imitation of Frerich's treatise, which he had translated for the Sydenham Society, but it is, nevertheless, strongly characterized by those qualities which impart to the clinical work of English physicians a peculiar value—conscientious observation, fidelity of description, and a happy faculty of inference, which has almost the force and fruitfulness of original discovery. The volume on diseases of the liver, the ninth of the series constituting Ziemssen's Cyclopædia, is the last to make its appearance, and, therefore, represents the newest phase of German opinion and practice. As this volume is the combined work of Ponfick, Thierfelder, Von Schueppel, and Heller, it may be accepted as a satisfactory exposition of the subject from the standpoint of German thought. But our duty is, more especially, to present to our readers an adequate conception of the work of Dr. Legg; to show how far successful he has been in the account he gives of our present knowledge, and to what extent he has enlarged the boundaries of our existing information. Dr. Legg must, we fear, be classed rather with the iconoclasts, and, as these terrible medical skeptics usually do, shatters ruthlessly our most treasured notions. But like all idol-breakers, he is more apt at destruction than at building up, so that one peruses his work with a definite sense of the waste of experimental inquiry, devoted with so much assiduity during ages to the elucidation of the hepatic functions. The reader, also, realizes that this ponderous tome, filled with vast and varied learning, is simply a record of mistakes, contradictions, and failures, and that a genuine knowledge of the functions of the liver is yet to be acquired. In the practical part of the work, we pass, it is true, from the domain of experiment and speculation, and find that here, at least, something is definitely known, but the same spirit of pessimism dominates fact, or supposed fact. In a single sentence he disposes of functional hepatic affections, on which Murchison delivered a course of lectures very recently, and which have occupied a large space in humoral pathology, from the time of Galen down. "Now," says Dr. Legg, "if we were to ask modern science what diseases were caused by the bile, all the answer would be jaundice and gall-stones; about any other nothing is known" (p. 662). To estimate with an approach to accuracy the formal opinions of any writer, we must know something of his psychological state, of the influences which have surrounded him and gradually made an impression on his modes of thinking and acting. Especially is this necessary in the case of Dr. Legg, who sums up, it is true, with judicial gravity the knowledge of all times, but his opinions are always coloured by a prevailing pessimism. We find in his book, unconsciously portrayed doubtless, the sources of his skepticism, the inspiration of his iconoclasm. "I am not one of those," he says (p. 664), "much tempted to follow the newest fashion in medicine; or in philosophy, morals, and religion; and still less in names." He tells us in his preface that he "has not fallen into the un-English virtue of consistency," and that "whatever imperfections there may be in the method followed, the reader must blame those Manichæan teachings, which, harmful as they are, are almost as old as the human race itself, and the germs of which seem to exist everywhere, ready to burst into a fresh life, even amongst those who claim to be most orthodox and sincere in their morals and belief." The work is dedicated to Prince Leopold in the usual loyal manner. From these characteristics, we may construct the mental type of the author, as the comparative anatomist does an extinct animal, from a few bones. He is a stanch tory, we doubt not, deeply imbued with the ideas of his class; his temperament melancholic, or bilious, if we may still use the much condemned phrase, and his modes of thinking, therefore, rather gloomy than sanguine. With him the illusions of life go for little, and what is called human knowledge seems to him little more than idle speculation. We must judge of his work, then, by the illumination afforded us in this glimpse of his mental and moral characteristics. But the reader must not suppose that we undervalue the work because we draw a rather unsympathetic picture of the workman. Dr. Legg's treatise is a really great book, exhibiting immense industry and research, and full of valuable information, as we will see, as we advance further in its examination; but we must not lose sight of the type of character producing it. Taking up this work then, in order, we will pass in review the several parts.

Dr. Legg treats only of the bile and the biliary diseases of the liver, and does not include in his account of the functions of the organ the glycogenic, although constant references to the glycogen become necessary. His account of the chemistry of the bile is very full, and in the consideration of this topic his spirits do not fall so low, since in this respect our knowledge is more complete and exact than in any other connected with the liver. The bile contains certain acids—glycocholic and taurocholic—combined with soda; pigments, bilirubin and derivatives, and fats, chiefly cholesterin. The acids are not the same in all classes of animals, although closely allied. According to Strecker, whose researches are confirmed by Hoppe-Seyler, the nitrogenous bases of the bile acids are always the same —glycocoll and taurin. The acids of the bile are the largest and doubtless the most important of its constituents. Their origin must, therefore, have an important bearing on the question of the sources of the bile. As they cannot be detected in the blood, and have not been, according to the most recent researches, they must be formed in the liver. Next to the acids, the pigment of the bile is a peculiar constituent. Much confusion has arisen from the variety of names given to this colouring matter. Berzelius first entitled it cholepyrrhin, Simon biliphaein, and Städeler bilirubin, which has become the most generally adopted name, and is employed by our author. Bilirubin is converted by oxidation into biliverdin, which is the green pigment of the bile of herbivorous animals, and is also present with bilirubin in human bile. These two pigments are universally admitted to exist, but Städeler asserts that various pigments, named by him bilifuscin, biliprasin, bilihumin, and bilicyanin, are also to be found, but thus far he stands alone in this assumption. Various secondary products are obtained from bilirubin by the oxidizing action of nitric acid, which constitutes Gmelin's test. When bile is brought into contact with nitric acid, the yellow colour quickly changes into green, then blue, violet, red, and finally into a dull yellow. When bile is cast up by vomiting, it quickly becomes green by exposure to air, and sometimes this change takes place in the stomach. All of the pigments represented in this play of colours have been isolated. A very important question connected with the bile pigment is, whether it is preformed in the blood, and merely separated by the liver, or constructed in this organ. Opinions differ. Ponfick affirms (p. 9) that bilirubin is found in the blood, and the bile acids alone are produced in the liver. On the other hand, Legg says that the bile pigments are found only in the liver and in the bile (p. 85). It is difficult to account for Ponfick's blunder, since the analyses of Lehmann, of Hoppe-Seyler, and others, afford conclusive evidence that the blood of even the portal vein does not contain a trace of these pigments. The importance of this question is enhanced by the relationship which may exist between the blood colouring matter and the bile pigment—a topic which underlies the subject of hæmatogenic jaundice.

> "The relation of the bile pigments to the colouring matters of the blood is that which has the greatest attraction for the physician, inasmuch as much of the doctrine of hæmatogenous jaundice depends upon the belief that the two bodies are the same. Doubtless, the idea that hæmatoidin and bilirubin are identical has much to recommend it to the notice of physiological chemists, but the notion has, I think, been asserted with scarcely sufficient proof. It is, however, an example of the rashness which characterizes the present generation of physiological chemists; they make up for the extreme uncertainty of their opinions by an increased boldness of assertion."

After an elaborate examination of the rather conflicting observations, Legg concludes that the identity of the two substances is disproved. Both

Kühne and Hoppe-Seyler, however, regard them as identical, and use the terms hæmatoidin and bilirubin as mutually convertible.

Although cholesterin, the principal fat in the bile, is widely distributed throughout the organism, it is probably formed in the liver. Such is the view of Beneke, supported by the chemical examination of Drosdoff, who found four or five times as much cholesterin and lecithin in the blood of the hepatic as of the portal vein. Lecithin is a fatty body containing phosphorus, not unlike Liebreich's protagon, and is a constituent of the bile. Our author is by no means a believer in Flint's doctrine of cholesteræmia. The readers of this Journal need not be told that Dr. Flint, Jr., regards cholesterin as an excrementitious substance entirely, and that it is an important function of the liver to secure its excretion. Flint is by no means without able support of his doctrine. Thus, Beneke holds that the excretion of cholesterin is a function of great necessity to the economy, but he does not go as far as Flint; on the contrary, he maintains that this substance, in company with its congener, lecithin, passes into the intestine with the bile, and is thence widely distributed throughout the body. Flint, however, maintains that cholesterin (he takes no note of lecithin) passes out with the feces, in the form of a substance styled by him *stercorin.* The retention of cholesterin, by reason of the failure of the liver to excrete it, according to Flint, causes cerebral disturbance like that of uræmia, and hence he entitles the complexus of symptoms produced by this retained excretion, *cholesteræmia.* Unfortunately for this theory, it has been found that the injection of a solution of cholesterin into the blood does not cause any disturbance of the system.

In Chapter IV. our author enters with some particularity into the physical and chemical characteristics of human bile. It is but rarely that human bile can be obtained in a fresh state free from any foreign ingredient. Of biliary fistula in dogs, we have had an abundance, but, for obvious reasons, it is very desirable to have an accurate standard of healthy human bile. But a single example of such a fistula in the human subject, free from any source of erroneous interpretation, has been recorded. This was a case of operation for empyema, the escape of pus being followed after some days by bile, which continued to flow for a fortnight, the feces for the same period being colorless. The case was reported by Westphalen, and the bile was examined by Jacobsen and Von Wittich. Legg sums up as follows our present knowledge of the physical and chemical characters of human bile, and as it is an excellent statement of facts, our readers will, no doubt, be pleased to have it placed before them:—

> "Freshly secreted bile is a fluid—not viscid, of a golden-yellow, brown, or green colour; its reaction is usually neutral, sometimes barely alkaline; its specific gravity about 1010. It contains about two to three *per cent.* of solid matter, and has the power of changing starch into sugar. This power is lost if the bile remains long in the gall bladder; it then shows a deeper colour, is brown, and is of higher specific gravity, 1030 to 1040, and becomes viscid from the presence of mucus. The amount of solids in this cystic bile varies from eight to seventeen *per cent.*, but the relation of these solid constituents to one another does not seem to vary.
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> "The soda salts of the bile acids make up about one-half of the solid constituents; they may, however, vary from forty to seventy *per cent.* of the solids. It is known that these bile acids are formed by a combination with glycocoll and taurin, but whether the cholalic acid of man be identical with the cholalic acid of the ox is not known. It is certain that a taurocholic acid exists in the bile of man, although now and then it may be entirely absent, the glycocholic acid

being usually the dominating acid. This forms about three-quarters of the soda salts of the bile acids, while taurocholic acid forms the remaining quarter.

"It is known that bilirubin and biliverdin exist in human bile; the other bile pigments have not been found. Their amount has not been directly estimated. With mucus, it is thought to be from ten to fifteen *per cent.* of the solids.

"The fatty matters, the cholestearin, the soaps, and lecithin, make up from three to twenty *per cent.* of the solids. They seem to vary inversely with the amount of inorganic salts. The salts may be from fifteen to thirty-five *per cent.* of the solid bile; and of these salts, about two-thirds are made up of chloride of sodium. The remainder consists of phosphate of soda and lime, carbonate of soda, chloride of potassium, traces of magnesia and silica, and constantly traces of iron and copper. Urea, sugar, leucin, tyrosin, and albumen, are not found in health in human bile."

What is the source of the bile? Is it an excretion, or a secretion? That these questions yet remain for solution, seems extraordinary. An almost incredible amount of research has been devoted to the elucidation of the subject, and our author truly says, the results are so contradictory that we must needs fall back on the general principles of physiology. It has already been pointed out that the bile acids and pigments are not to be found in the blood, and hence the presumption is they must be formed in the liver. But, again, it is now known that these acids and pigments can be detected in minute quantity in normal urine, whence it is concluded that they must have existed in such minute quantity in the blood as to escape detection by our present means of research. But this fact does not obviate the difficulty, for these substances may have entered the circulation from the intestinal canal. As during the existence of jaundice these acids and pigments can be readily found in the blood, it would seem that if they were present in health they could hardly escape detection. Reasoning in this way, it appears conclusive that bile is a secretion, and that it is not merely separated from the blood, as Glisson taught, the liver acting merely as a sieve. Whether the blood of the portal vein or of the hepatic artery furnishes the material for the formation of bile, has been disputed with great persistence. Legg concludes to leave the subject where Bichat left it—that is, to be decided by future investigation, so it would appear that we are no nearer a solution of this problem than they were in Bichat's time. The actual amount of bile secreted can only be approximatively determined. In Westphalen's case of fistula in man, in which bile was discharged externally for two weeks, none apparently appearing in the feces, the daily amount of *solid* bile was about ten grammes, or one hundred and fifty grains. In another case of fistula in man observed by Johannes Ranke, in which admixture of foreign matters with the bile occurred to a greater or less extent, the quantity of *solid* bile was about twice the estimate in Westphalen's case. But this estimate, it is interesting to note, corresponds closely with the amount determined by Bischoff by comparison with results obtained by observations on animals.

The quantity of bile secreted is subject to great fluctuations. It is diminished by fasting; it is increased by taking food. The maximum secretion takes place some hours after food; according to some observers in four, according to others, in eight hours after eating. It seems clear, although there is some contradictory evidence, that more bile is secreted on a nitrogenous diet than on one of fat or of starch. An increase in the blood-pressure raises the production of bile; a diminution in the blood-supply and active muscular movements lessen the quantity of bile. The effect of irritation of the spinal cord, before division of the splanchnics, seems to be inconsiderable—at first, the flow of bile seems increased, then lessened, but no change takes place, after these nerves have been divided. The very interesting and important fact, first observed by Bernard, that irritation of the orifice of the bile-duct in the duodenum with acid caused a great flow of bile, explains the outpouring of bile which occurs when the acid chyme enters the intestine.

In his chapter on "the office of the bile," Dr. Legg makes some satirical observations on the very contradictory statements which have been put forth by physiologists:—

> "After the bile has been poured into the duodenum, and done whatever it is appointed to do, whether it be a positive harm to the process of digestion, a suggestion which in the present state of knowledge may be entertained; or be simply an indifferent fluid; or in some way aid the pancreatic juice; what becomes of the humour? Does it pass entirely out of the body with the feces, or is it absorbed again into the circulation?" (p. 147.)

After a discussion of the changes supposed by modern physiologists to take place in the bile when it reaches the intestine, he again remarks, in a despairing tone:—

> "To what purpose then serves the bile? It cannot be looked upon solely as an excrement, for it has been seen what deep changes in nutrition follow its diversion from the body. There is no evidence that it is necessary for the completion of the process of digestion in the stomach or intestines; indeed it may be said by some physiologists that it does harm to the process in either viscus. The view that it acts as a sort of natural purge has little against it, but, at the same time, there is but little in its favour. As to the power of the bile in arresting putrefaction, it would seem that it must be small, if, as soon as it arrives in the intestines, it begins itself to undergo putrefactive changes. The view that the bile neutralizes the acid of the chyme must fall with the establishment of the fact that the bile is not alkaline but neutral in reaction. The only office which remains to it, is that of emulsifying fats, a property known to the Greeks 2200 years ago, and of changing starch into sugar. It is melancholy to find that in so many years nothing more is known with certainty as to the uses of this long-studied humour.
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> "It has seemed to me that physiologists are drifting into the belief that the office of the bile is not to act upon the chyme or to assist in the first digestion of aliments. Rather its office is to pass into the intestine, there to undergo changes itself, the products of decomposition being absorbed into the blood, and leaving the body by the urine. If it be admitted that the bile acids be decomposed before they be absorbed, it is most probable that they split up into glycocoll, taurin, and cholalic acid. The glycocoll, it has been seen above, is one of the bodies which, when taken into the intestine, appears in the urine as urea; taurin, in like manner, appears in the urine, probably furnishing the unoxidized sulphur of this secretion, though, according to Salkowski, it can no longer be thought that in man it is the source of the oxidized bodies, the sulphates. The cholalic acid would appear to leave the body by the feces; but a theory might be made by adopting Schiff's view of a circulation of the bile; supposing a salt of cholalic acid to be absorbed and conveyed to the liver, and there to unite with freshly-made taurin and glycocoll, and again to be excreted by the bile. Of the destiny of the bile pigments, little has yet been said; by some it is thought they undergo oxidation in the intestines; by others reduction; but the product of the change, whatever it may be, is called by Valair and Masius stercobilin; a pigment which is closely allied to that colouring matter of the urine, named urobilin by Jaffe. It thus becomes possible that the bile pigments after suffering whatever chemical changes they may be destined to undergo in the bowel, are absorbed into the blood and excreted by the urine as colouring matter, while the remainder passes out with the feces. The end of the bile would thus seem to be excretion by the urine; a view not altogether new, for it was taught by physiologists, sixteen hundred years ago, that the urine was formed in the liver and separated by the kidneys." (pp. 155 and 156.)

We have in this extract a specimen of Dr. Legg's style, and of the pessimistic spirit in which he regards the present state of the physiology of the bile. Of his industry in accumulating the so-called facts of physiological chemists, of his candour in expressing his doubts, there can be no question. But he has not entered the field of research for himself to attempt the elucidation of controverted points. It is true, the absurd anti-vivisection law has almost stopped physiological research in England, and our author, in his preface, acknowledges his obligations to the French authorities for permitting him to use the great laboratory of the veterinary school at Lyons. Yet the researches undertaken were not occupied with these obscure questions in regard to the sources and final disposition of the bile. It will be profitable to inquire, briefly, as time and space are inadequate, if our author, influenced by his dominating skepticism, has not rather underrated what is actually known of the office of the bile in the intestine. May we not here, in view of the contradictory statements, fall back upon certain general principles, as our author recommends under analogous circumstances? Some offices of the bile appear to be well understood. It has an antiseptic effect, and prevents the decomposition of certain foods whilst in the upper part of the small intestine. In this instance physiological experiment is in accord with clinical observation. Who does not know that when bile fails to reach the intestine, the stools are fetid from putrefactive decomposition. Bile assists the pancreatic secretion emulsify the fats, and powerfully aids the passage of "the molecular basis of the chyle" into the lacteals. It has been experimentally proved that oils pass through animal membranes and through plaster, wet with bile, with much greater facility than when wet with water merely. Wistinghausen first demonstrated this, and his experiments have been confirmed and extended by Dr. Williams in this country. Sir Benjamin Brodie, and afterwards Magendie, showed that when bile was diverted from the intestine, by a biliary fistula, fat did not enter the lacteals; except in very small amount, was afterward shown by Bidder and Schmidt. The last-mentioned observers also found that the fat largely escaped absorption and appeared in the stools. All the world knows what Schwann, afterwards Bidder and Schmidt, also ascertained by direct experiment, that when the bile is diverted from the intestine, the nutrition fails remarkably, and death ultimately ensues. Now and then, by the obstruction of the hepatic duct by a calculus, a pathological experiment is effected in man, the conditions of which are the same as when a biliary fistula is made in a dog, and the results as regards the nutrition and the failure of the vital powers are the same. Thus, as respects the disposition of fats, is the bile seen to have an important function. But this is really but a small part of the current knowledge of the hepatic functions.

Dr. Legg does not extend his inquiries to another important function—the glycogenic—although he makes necessarily many important allusions to its connection with the biliary. Since the discovery by Bernard of the glycogenic function of the liver, there have been numerous investigations in regard to the source, nature, and functions of this substance. Have we any exact knowledge on this point? It must be admitted that we have more speculation than actual information, but some things are known of which Galen could hardly have dreamed. Our readers are doubtless familiar with the discussion which has taken place, as to the seat of the production of glycogen, and its relation to, or independence of, the biliary function. Bernard held that the two functions were independent, and some of his followers, that certain hepatic cells secrete bile, and others glycogen. Pavy, the English physiologist, maintains that glycogen is found in the liver as a post-mortem change; and Flint, in papers with which our readers must be acquainted, has shown that it is present at the shortest time possible for the most expert operator to obtain a portion of the organ for examination. Recent researches, especially those of Kühne and Heynsius, have proved that the two functions are intimately associated, for if the bile be diverted from the intestine, the glycogen is greatly decreased in amount, or disappears from the organ entirely. New light on the origin and office of glycogen has been cast by late researches of Pavy (*Lancet*, July 2 and 9, 1881), who has shown, contrary to existing belief, that glycogen is not converted to any appreciable extent into sugar in the blood, and that it exists as a normal constituent in that fluid. He finds it very widely distributed throughout the organism—"occupying a parallel position to albumen, viz., existing in the colloid state, and thus adapted for retention within the body, instead of passing off as a diffusible substance like glucose tends to do." Its importance as a ready means of producing force seems to be indicated in these facts, and here we certainly have important light cast on the functions of the liver.

Dr. Legg devotes a chapter (VIII.) to the actions of drugs on the secretion of bile. We find no new observations on these remedies; but he faithfully records the observations which have been made by others, including those on Westphalen's human subject, Scott's, who first studied the effects of supposed cholagogues on dogs with biliary fistula, Rohrig's, the Edinburgh Committee's, and especially Rutherford's. Whilst there are minor exceptions, on the whole there is a remarkable unanimity in the results of these investigations. It can no longer be said, that the effects obtained by experiment on dogs with biliary fistula, are not applicable to man. In Westphalen's case of human biliary fistula (*Deut. Archiv für klin. Med.*, Band xi. p. 598 *et seq.*) a dose of twenty grains of calomel rather decreased the amount of bile discharged. This is the uniform result of the action of purgative mercurials, except corrosive chloride in dogs. Purgatives generally lessen the flow of bile, but the resin-bearing cathartics, as a class, have distinct cholagogue effects, although they vary in the degree of the action. The following list includes the substances having a distinct power to increase the flow of bile:—

"Aloes
Podophyllin
Rhubarb
Colchicum
Colocynth
Jalap
Ipecacuanha
Benzoates
Salicylates
Sulphates of potash and soda
Phosphates of soda and ammonia
Dilute nitrohydrochloric acid
Corrosive sublimate
Muscarine
Nicotine
Physostigma
Euonymin
Sanguinarin
Iridin
Leptandrin
Baptisin
Photolacin
Hydrastin
Juglandin."

In this list we recognize remedies which have long been known to stimulate the hepatic functions, and others are equally conspicuous by their absence. Thus possessed of a group of remedies, which may be justly regarded as cholagogue, the question arises, What will we do with them?

> "It has been seen," says our author, "that the wish to increase the amount of bile excreted by the liver comes of a most venerable antiquity; but it may now be asked, in what diseases or in what states would good be done to a patient if the amount of bile poured into the duodenum were increased? It seems to me that it would be judicious to put aside at once all organic diseases of the liver, such as cirrhosis, amyloid degeneration, and the like; for in them the same kind of evil would follow the use of a stimulant to the liver, as of certain diuretics in Bright's disease. . . . Then in cases of jaundice, it would surely be undesirable to attempt to increase the secretion of bile; for the bile passages being already overfilled, harm would be done by pouring fresh bile into them. Then comes the long list of disorders, which the public love to think due to 'the bile,' and called 'biliousness,' the symptoms of which are really due to a catarrhal state of the gastro-duodenal mucous membrane as will be seen in the chapter on bilious disorders."

Our author, indeed, can conceive of no condition in which stimulation of bile-flow may be desirable, except "at the end of an attack of jaundice when the stools have begun to show some appearance of returning colour, but the conjunctiva, skin, and urine of the patient still remain yellow."

As the subjects of biliousness, so-called, and the action of cholagogue medicines, are important practical topics in this country, especially through the west and south, it may be desirable to develop at this point, the real state of scientific opinion on these questions. Dr. Legg devotes the last chapter of his work to "Bilious Diseases," but clearly, this department of the subject has close relation to that which we are at present considering, and may therefore be appropriately taken up now. The existence of bilious diseases, and the belief in biliary derangements, in too little or too great supply of bile, are deeply rooted in the convictions of men, and have been, from the time of Hippocrates, in whose system various kinds of bile played an important part. Bartholin was the first of the modern school to dispute the Galenical views. But, as has been pointed out, the reaction has gone in the opposite direction, and now various conditions of the bile are, in common professional and popular belief, influential agents in disease production. The swing of the pendulum of professional beliefs is again starting away from this point, and the "bilious state," and "biliousness," are strongly doubted as morbid entities by the new school of physiological physicians. Frerichs treats of hyperæmia of the liver due to gastro-intestinal catarrh, but we do not find in his work any references to the functional disturbances of the liver such as in England and in this country are supposed to exist under the term biliousness. Murchison, in his very suggestive and interesting Croonian lectures, holds to the belief in such derangements. A large portion of the physicians in this country, especially those practising in malarious regions, are unquestionable believers in biliousness, as a distinct morbid state. Our author, Dr. Legg, maintains, that "there is no evidence that the disease is accompanied by any increase or decrease, or any change whatever, in the secretion of the bile." His view, that the condition is really gastro-duodenal catarrh, is probably correct in large part; but not every case of this kind is accompanied by a muddy complexion, yellowness of the sclerotic, and light-coloured stools, indicating biliary derangement. There are two forms of the condition, then—one limited to the gastro-duodenal mucous membrane; the other, accompanied by signs of biliary derangement, and therefore, doubtless, extending to and involving the orifice of the *ductus communis choledochus.* In the latter sufficient swelling of the mucous membrane about the orifice of the duct exists, to hinder, to a greater or less extent, the escape of bile into the duodenum, although not to prevent it entirely. During many years of practice in malarious localities, the reviewer saw numerous examples of this form of gastro-duodenal catarrh, or biliousness. When, in such cases, the whole tract of the hepatic duct is involved, we have the well-known catarrhal jaundice, which, for obvious reasons, is much less apt to occur than catarrh limited to the duodenum. By Murchison (p. 565) symptoms of the same kind are referred to *lithæmia*, that is, imperfect oxidation, the accumulation of uric acid and urates in the blood, and their excretion by the urine. Murchison admits that "these symptoms are the more likely to occur if the patient be what is commonly known as a 'generous liver,' if he takes little exercise in the open air, or if he have much mental work." The complexus of symptoms, given by him, are those of gastro-duodenal catarrh, and he enumerates amongst them, weight at the epigastrium, flatulence, heart-burn, a furred tongue, metallic taste, headache, change in the colour of the stools, etc. It can scarcely be doubted that Murchison has ascribed to lithæmia the symptoms belonging to gastro-duodenal catarrh, and that he confounds effects with causes. The final conversion of nitrogenous materials into urea, is the work of the liver, it is true, probably, but when gastro-duodenal catarrh exists, the peptones are imperfectly prepared, and here is the first step in the morbid process.

In determining the bilious state, much assistance is usually afforded by an inspection of the stools, but all modern authorities are agreed that this information may be very misleading. Legg says:—

> "To tell the truth, very little knowledge exists as to the cause of the colour of the feces, either in health or in disease. It is indeed known that a few drugs, such as iron or bismuth, blacken the stools, and that complete obstruction to the common duct will cause them to become clay-coloured; but the other causes of the varying colours remain almost unknown The only proposition that can be safely upheld is, that bile is not the sole cause of all the change in colour." (p. 661.)

As far as the condition of biliousness is concerned, the change in the colour of the stools is eminently characteristic and can be referred to the absence of bile.

Next to the belief in the existence of biliousness as a distinct morbid state, is the conviction of a large portion of the medical profession in Great Britain and this country, that mercurials, particularly blue pill and calomel, are especially effective in removing it, and restoring the normal. No point in therapeutics has been more fully discussed, and, hence, it deserves careful consideration at our hands. The evidence that calomel and blue pill do not increase but diminish the secretion of bile, has already been placed before the reader. But two facts directly bearing on the question at issue, are now well-established: the stools are changed in character by mercurials; the symptoms of biliousness, or gastro-duodenal catarrh, disappear under their use. If these remedies, then, do not act on the liver, how explain their good effects? We believe, and have of late years taught, that the explanation is as follows: The colour and odour of the stools begin to have their usual characteristics in the lower part of the ileum and especially in the cæcum. Mercury increases the activity of, and is largely eliminated by, the enormous glandular apparatus of the ileum and cæcum, and to this action is to be referred the change in the colour of the stools. Small doses of calomel ($\frac{1}{20}$ to $\frac{1}{4}$ grain) have a remarkably sedative effect on the gastro-intestinal mucous membrane, just as powdered calomel will allay an inflammation of the conjunctiva. Other remedies act favourably—the salines for example—and all the world knows the good effects of a rigid diet and of abstinence. Since his demonstration of the cholagogue action of euonymin, Rutherford speaks strongly in behalf of a dose of this substance at bedtime and followed by a saline in the morning.

As "bilious" is a misleading term, Legg urges that its use be discontinued. (p. 663.)

In Chapter IX., Dr. Legg gives an interesting account of the physiological action of the bile, in the course of which he introduces a good deal of experimental evidence. This is a comparatively recent subject. Frerichs, in an appendix to his work, records the results of various experiments, but great progress has been made since in the knowledge of the physiological action of the bile. Röhrig, Kühne, Hünefeld, Traube, and many others, have contributed facts. As the effects of the bile, studied physiologically, serve to illuminate various points in hepatic pathology, and have therefore an immediate practical application, it may be desirable to summarize the ascertained facts. Bile exerts a solvent action on the red blood-corpuscles, but this result is due to the bile acids and not to the pigments. Muscles lose their contractility when acted on directly by the bile acids, but this effect is chemical, and does not occur when they are acted on through the blood. It is well known that the pulse of jaundice is slow, and much experimental work has been done to prove the cause. By Traube and Ranke this effect was attributed to the action on the muscular tissue, and by Röhrig, on the ganglia of the heart. The conclusion of Röhrig has since been confirmed by the experiments of Steiner and of Legg. As regards the influence of the bile acids on the blood pressure, much depends on the vessel into which they are introduced; when injected into the jugular vein, the pressure falls, and when injected into the carotid artery the pressure rises. No conclusions can be safely drawn from such observations. The temperature is decidedly reduced by the bile acids. On the brain, they act as a narcotic, causing drowsiness and stupor, and they lower the reflex function of the spinal cord. The cerebral effects caused by the bile acids should be carefully distinguished from the symptoms due to thrombosis of the pulmonary artery when the bile acids are thrown into the jugular vein. The bile pigments seem to be physiologically inert.

Thus far we have been occupied with topics which merely prepare the way for the consideration of hepatic diseases. Much of this has been physiological and speculative, yet we will find at all points that the obscure problems waiting for solution are closely connected with the most practical questions.

Frerichs, as is well known, opens up the subject of liver diseases by discussing jaundice as a symptom. Dr. Legg approaches the subject in the same way, and in Chapter X. discusses the etymology, history, and etiology of jaundice. Jaundice may depend on several conditions. In the first place, it has been assumed that it may be produced in the blood by changes in the colouring matter—hæmatogenous jaundice—as for example, the jaundice in pyæmia and putrid fevers. According to one view, the liver merely separates the bile from the blood, and hence jaundice may be produced when the organ can no longer perform this office. The third, and most generally accepted view is that which ascribes jaundice to the absorption into the blood of bile previously formed by the liver. The subject of hæmatogenous jaundice possesses a high degree of interest.

Although not wholly a modern theory, Virchow may be regarded as its real founder. There are many reasons for a belief in the existence of this form of jaundice, chief among them being the close resemblance of hæmatoidin and bilirubin. As is usual, physiological chemists of equal eminence, differ as to the identity or resemblance of these substances. Virchow, Funke, Valentiner, and some others, maintain that in crystalline form and in reaction,, the two bodies are the same, but, on the other side, Strädeler, Preyer, Holm, and others, affirm that they differ in these respects, and especially in their spectra, which are widely apart. If there be an identity in composition and structure between hæmatoidin and bile-pigment, the introduction of any agent into the blood which would set free its colouring matter, must result in the production of jaundice. This has not been accomplished. Various agents set free the hæmoglobin, but jaundice has not followed, although the bile-pigments, it is said, appear in the urine. But this point is also disputed. Frerichs, Kühne, Munk and Leyden, found that the bile-pigments were present in the urine, but J. Steiner and Legg were unable to detect them under the same circumstances. The confusion is probably due to the fact that the blood-pigment reacts in a similar manner to bile-pigment, and still more, to the fact that in dog's urine there is normally present a substance which reacts in the same manner as bile-pigment. After a careful survey of all the evidence, our author concludes as follows :—

> "The grounds on which the theory of hæmatogenous jaundice have been set up are, to my mind, altogether insufficient. It cannot be said that the origin of the colouring matter of the bile, from that of the blood, is proved; indeed, of late, the course of discovery has been rather against their identity than in favour of it. And until it has been shown that bile pigment has its source in the blood-corpuscles, it will be the duty of the practical physician to reject the theory of hæmatogenous jaundice."

Frerichs came to similar conclusions twenty-five years ago, and urged similar reasons for rejecting this theory.

> "As regards the spontaneous conversion of the red matter of the blood into bile pigment in putrid diseases, no objection can be made to the possibility of such an event, considering the intimate relations which have been shown to exist between hæmatine and cholepyrin [bilirubin]; but positive proofs of it are wanting. As yet no one has succeeded in manufacturing bile pigment from the red colouring matter of the blood, although the products of decomposition of both are the same. The yellow matter, however, which in cases of pyæmia circulates with the blood, and is voided in the urine, is at least in most cases identical with bile pigment, and participates in all the properties of this substance. But even were the conversion of hæmatine into bilirubin, under the operation of certain agencies possible, still it remains to be proved that this metamorphosis really takes place in the course of putrid diseases within the bloodvessels of the living body." (Vol. i. p. 84.)

The labours of twenty-five years have, therefore, not cleared up the doubts; only it may with justice be said that the great mass of experimental inquiry has not been wholly in vain, since the doubts regarding the existence of hæmatogenous jaundice have increased. The results of physiological research have, however, not been so barren in that form of jaundice known as jaundice by suppression. It has been held, quite down into our own times, by Bamberger, Trousseau, Budd, and more recently by Moxon (*Transactions of the Pathological Society of London*, vol. xxiv. p. 133 *et seq.*), that the bile is formed in the blood, and merely strained off by the liver; hence, jaundice results when the liver is incapacitated from the performance of this function. We have already given the experimental data which negative this theory. Neither the bile acids nor the bile pigments have been found in the blood, not even the blood of the portal vein. The third theory of jaundice is that which supposes an absorption into the blood of bile already secreted by the liver, some obstacle existing to prevent the passage of the bile into the intestine. This theory best harmonizes all the facts, and is now universally admitted to be true.

Very little obstruction suffices to pass the bile into the blood, rather than into the duodenum. It is not necessary that the duct be closed; if there be some swelling of the mucous membrane so that the flow of bile is impeded, it is sufficient to start the flow into the blood. From this fact we get a clear understanding of the varying degrees in which with gastro-duodenal catarrh there may be implication of the biliary function. Jaundice may also be caused by a considerable diminution in the pressure of the bloodvessels of the liver. Frerichs advocates this theory. It is assumed that the bile passes in the direction of least resistance, which will be towards the vessels, when the blood-pressure is low. This fact has been experimentally shown by Heidenhain, and such is the mode of explaining the jaundice caused by mental emotion, by bites of serpents, and by loss of blood.

In Chapter XI. our author treats of the symptoms of jaundice, and in Chapter XII. of the complications. We pass over these, although full of interesting matter and rich in suggestion, except to mention merely that he gives an excellent account of Xanthelasma, illustrated by a beautiful chromo-lithograph. In Chapter XIII., on the morbid anatomy of jaundice, we find several subjects of recent development, which have an important bearing on practice. We should not fail to direct the attention of our readers to these points. We refer to the histological changes which take place in the liver consecutive to obstruction of the ducts. These changes have been studied by Charcot, and by Legg (the latter is, we believe, entitled to priority), by experiments on animals, as well as by observations on man. Before Legg's special studies were undertaken, Oskar Wyss had, however, distinctly referred to the changes which take place in the interlobular connective tissue (*Virchow's Archiv*, Band 35, p. 553; *Beitrag zur Histologie der icterischen Leber*). Dr. Legg, with characteristic fidelity, refers to these observations, and assigns them their proper position, notwithstanding they barely relate to changes which he has laboriously described. There is, doubtless, some amiable sarcasm hidden in the following paragraph:—

> "The histological changes of the liver in obstruction to the duct had been until lately but little studied, though at Paris we are told that within the last three years the subject has become the order of the day. This is no doubt owing to the experiments of Charcot on this point, which have everywhere drawn much attention."

Catarrh and dilatation, to a greater or less extent, of the ducts, pigmentation of the liver, and jaundice of the hepatic cells, have of course been pretty thoroughly described. As regards the changes of the connective tissue, its overgrowth and the consequent hypertrophic thickening and enlargement of the organ, caused by obstruction of the bile ducts, we owe the first important studies to Dr. Legg, who was soon followed by Charcot in the same vein. These changes may be but trivial in temporary obstruction of the ducts, but in long-standing cases they become considerable. Dr. Legg finds that in dogs, whose common duct is tied, the overgrowth of connective tissues goes on rapidly, and attains extensive proportions. The explanations which have thus far been brought forward of this hyperplasia have not been satisfactory.

The changes caused by obstruction are not limited to the connective tissue. The hepatic cells participate. Leyden describes fatty infiltration of the cells, and his statements are confirmed by Hayem and Cornil. Wyss, Meyer, Legg, Charcot and Gombault find that this fatty infiltration is not constant, and not so extensive as Leyden supposed. The cells waste and become granular, the protoplasm gradually disappears, and sometimes they have a shining, vitreous appearance. When the obstruction is permanent the cells may completely disappear, and are replaced by a granular and fatty detritus.

Although the mechanism by which these changes are wrought remains unexplained, the facts themselves have a high degree of clinical significance. We see in these histological changes an imperious necessity for the prompt removal of the causes of obstruction whenever it is practicable to do so. We learn further how successive attacks of duodenal catarrh, with swelling of the orifice of the common ducts (the simplest cause of obstruction) will, in time, bring about serious changes in the hepatic structures.

Characteristic alterations also occur in the kidneys in cases of jaundice. Legg finds that nothing can be added to the accurate account given by Frerichs. Besides the straining of the organ in various degrees, the epithelium of the tubercles is filled with pigment, and undergoes fatty degeneration.

In Chapter XIV., on the functions of the liver in jaundice, Dr. Legg introduces much valuable matter, which brings into sharp contrast the author's pessimism, and the appreciation of the rich results obtained by modern investigations. Dr. Legg considers in order the disturbing influence of jaundice over the hepatic functions, beginning with the glycogenic. This he regards as the most important of the functions. It is lessened in activity, or entirely arrested when the ducts are obstructed.

> "In all cases I found that whether the animal died within a few hours or a few days after ligature of the bile ducts, in all cases alike, glycogen was absent from the liver."

He is habitually cautious in applying the results of observations on animals to the conditions in man.

> "It becomes a question how far this fact in animals may be applied to jaundice in man, when there is sometimes evidence from the presence of colour in the stools that the obstruction to the duct is not complete. In these and other cases the phenomena seem best explained by supposing that the glycogenetic function of the liver is not altogether abolished, but rather impaired. Even in cases of simple jaundice the patient wastes and loses flesh rapidly, and this seems best explained by supposing a great impairment, if not destruction, of the glycogenetic function. Glycogen is always found in growing parts, and its importance to nutrition cannot be doubted."

It has already been shown that there is an intimate relation between the biliary and glycogenic functions—that they are interdependent. The presence of bile is necessary to the production of glycogen. As it has been shown that in jaundice the diminution in the production of glycogen is in proportion to the extent of damage suffered by the liver, so also in the same ratio does the bile-producing function of this organ undergo abatement. The quantity of bile acids and of pigment excreted by the urine is greatly below the production in health. The reason is, there is much less formed. After a time the jaundice may cease simply because the liver is unable to produce any more bile.

Another function of the liver impaired in jaundice is the heat function. Claude Bernard first demonstrated the important fact that the temperature of the blood in the hepatic veins is higher than in any other part of the body. The great production of heat is unquestionably due to the active chemical processes connected with the formation of glycogen and of bile. It necessarily follows, if these two functions are lessened in activity, or suspended entirely, the heat produced must be less. This view is confirmed by the well-known clinical fact that in jaundice the temperature is subnormal.

Our author, notwithstanding the pessimistic view he takes of the progress of knowledge in respect to hepatic physiology, admits the existence of a fourth function—that of sanguification. The blood of the hepatic vein contains very little fibrin, and will hardly form a clot; it contains a relatively larger proportion of red and colourless corpuscles, and the extractives and fats are present in greater quantity than are found in the portal. As in jaundice the relative proportion of red corpuscles is much decreased, this result may be ascribed to the interference with the process of sanguification, which occurs when the liver is diseased.

Passing over the diagnosis and prognosis of jaundice, which are the topics of Chapter XV., we come to the treatment of jaundice, which occupies Chapter XVI. In this chapter Dr. Legg's iconoclastic spirit has abundant opportunity. After giving an account of the method of treating jaundice, which he calls "rational," he deals some destructive blows against the "empirical treatment." His method, in brief, consists in a careful regulation of the diet, excluding fats, starch, and sugar; in the administration of the milder preparations of iron to remove the anæmia; in the use of salines and alkaline mineral waters, to increase elimination by the kidneys; and in attention to the skin, to maintain its functions. That this method of treating the most usual form of jaundice—the catarrhal—is *rational*, we fully believe. That it will yield equally valuable results in other forms of jaundice, we doubt. Dr. Legg condemns the use of purgatives, except a dose or two to remove constipation, and includes in his anathema calomel, and the so-called cholagogues of vegetable origin. He can see no good in remedies which stimulate the hepatic functions when there exists an obstacle to the escape of bile, or when disease has attacked the organ itself. In the present state of knowledge, these reasons certainly seem to be conclusive. He is equally opposed to the use of emetics, but has a friendly word for the mineral acids, because, probably, a rational explanation of their utility has been given in the experiment of Bernard, who found that the application of an acid to the orifice of the common duct in the intestine caused an active pouring out of bile.

From jaundice, a symptom, Dr. Legg passes to the diseases of the liver, beginning in Chapter XVII. with *icterus simplex*. This he defines to be a self-limited disease, of two or three weeks' duration, always terminating in recovery. In the discussion of the causes, he expresses doubts, as might be expected, in regard to the influence of emotional excitement. The historical examples of jaundice caused by anger, fear, sudden joy, and other mental and moral emotions, he thinks may be explained on other grounds. He does not at all allude to the influence of malarial infection. That simple jaundice, without febrile disturbance, is caused by the imbibition of malaria in some subjects, is a fact, which any one who has practised in the intensely malarious localities of the Mississippi Valley will substantiate. In certain other subjects, malarial infection will induce chronic splenitis (ague cake); also, without the objective phenomena of fever, and as the sole evidence of malarial toxæmia. Legg admits, with Frerichs, that in a considerable portion of cases the real cause of the jaundice is catarrh of the bile ducts, originating often, probably most frequently, in gastro-duodenal catarrh. In malarious regions, again, this morbid state is very common. But the paludal poison is not the sole factor in its causation. Gastro-duodenal catarrh is a result of excesses at table, especially in the use of highly-seasoned and rich dishes, and it is readily produced by the habitual indulgence in spirituous and malt liquors. We have already pointed out that biliousness, from the simplest case of indigestion so called, up to fully-developed jaundice, may, and does usually, depend on gastro-duodenal catarrh causing more or less obstruction against the escape of bile into the intestine.

The importance of catarrhal swelling of the mucous membrane, or blocking of ducts by mucous plugs, has been recognized from Van Swieten down. Among moderns, Virchow has done most to demonstrate the existence of catarrhal jaundice. Dr. Legg comes to the conclusion "that a catarrh is a common cause of jaundice, cannot, I think, be disputed; but that it is the cause of all cases of simple jaundice still lacks proof; a difficulty not likely to be overcome soon, as opportunity for examination after death is so rare." We venture to add, that this cause will be found in action in all cases of simple jaundice, although other factors may have a determining influence.

Simple icterus sometimes prevails as an epidemic, under circumstances usually indicating the presence of poisons generated by decomposing vegetable and animal matters. When uncomplicated it does not differ from the sporadic form.

The most interesting disease in the group of hepatic disorders, considered from the point of view of the disputed functions of the organ, is acute yellow atrophy. This disease is a pathological vivisection, in which the organ is summarily removed from its associated organs. The widespread confusion which then results affords us a conception of the place occupied by the liver in the system of man. This disease is, therefore, deserving of the exhaustive examination given to it by our author, who devotes to it 140 pages, or one-fourth of his work.

As is his custom, Dr. Legg, who is fond of philological disquisitions, first discusses the name, and the synonyms in various languages. He does not approve, strangely enough, of the name proposed by Prof. H. C. Wood, M.D., in an article in this Journal (vol. liii. p. 418), viz., *leucinosis*, because leucine is found in the blood in this disease, and he remarks, rather irreverently, "I am glad to find that in this he has no follower."

"Acute yellow atrophy is one of the rarest diseases known to man." There is good reason for believing that some of the reported cases were examples of phosphorus poisoning. This has seemed probable, since in undoubted cases of phosphorus poisoning, the chemists have been unable to detect this substance in the bodies of the dead. A heated controversy has been going on in Germany over this question. "Liebermeister and Ossikovszky assert that no distinction can be drawn between acute yellow atrophy, phosphorus poisoning, and yellow fever; Schultzen and Riess and Winiwarter declare that there exist certain means, both before and after death, for distinguishing between them." There must be an extraordinary similarity, nevertheless—a fact of high interest from the point of view of causes of this singular malady. This fact is of great importance in another aspect. Phosphorus is much and freely prescribed in medical practice, and children have a strange *penchant* for eating matches—whence the question of yellow atrophy or phosphorus poisoning might arise. The statistics of Frerichs and those collected by Legg, prove that the female sex is more liable to this disease than the male. In 100 cases collected by Legg, there were 69 women or girls. Thierfelder says there are "fully one-half as many more cases amongst women than amongst males." The period in life most liable is from 15 to 30. All concede that pregnancy is the most important predisposing cause, the greatest number of cases occurring in the sixth month. A local and family predisposition has been noted, also. That a peculiar poison generated under conditions and in a form now not known, is the real pathogenetic factor, seems highly probable, in view of the history and behaviour of the disease; still more because of the production of a precisely similar malady by phosphorus. Interesting as it may be to pursue this topic, we must rather devote our attention to this disease as a means of casting a much needed illumination on the functions of the liver. We have already stated that it may be regarded as a pathological vivisection. We must now form an adequate conception of the kind and degree of damage sustained by the organ, and compare the changed with the normal functions. Unfortunately for the deductions to be made as to the part enacted by the liver, this disease is a general disorder, in which the liver suffers in common with many other organs, but in a more complete degree than any other. The liver becomes small, flaccid, yellow, and fatty. Through the yellow are scattered islets of red tissue, firmer and tougher, and apparently more shrunken. In an advanced state of the disease, the hepatic cells entirely disappear, only granular detritus marking their site. During the progress of the changes, the cells become fatty, and, at the outset, before the liver has wasted or even changed materially in its appearance, the microscope must be invoked to make the diagnosis. Whether a hyperplasia of the connective tissue of the liver also occurs, is warmly disputed, the weight of authority being in favour of the position that an increase does take place, when sufficient time is afforded. The muscular tissue of the heart, the renal epithelium, and other organs and tissues undergo a similar granular and fatty degeneration. Without commenting on the obvious disturbances in the functions of the other organs, we consider the changes which ensue by reason of the cessation of the hepatic functions. If the disease is not advanced, some bile may still flow into the intestines, but in a great majority of the cases, Legg, as all other authorities, states that the stools are grayish or clay-coloured; or they may become tarry or blackish, says Frerichs, from admixture with blood. Thierfelder makes the same statement, although he admits that "occasionally" they may be bilious. Here, indeed, Dr. Legg expresses an opinion in conformity to common experience, but at variance with his earlier observations, on which we have commented, namely, that the stools afford no indication of the presence or absence of bile. As the disease is of short duration, all of the bile produced flows into the blood, and the jaundice persists until death. If the disease were more protracted, and the liver suffered the same damage, there would come a time when the jaundice must cease, for, the bile being no longer produced and the kidneys continuing to excrete it, all would disappear. The excretion of bile pigment must, however, be slow, in a disease in which the renal tubular epithelium is so quickly disintegrated. The conclusion which physiological chemists have, provisionally, at least, reached in regard to the bile acids, is that they are split up in the intestines into glycocoll, taurin, and cholalic acid; the glycocoll is excreted by the urine as urea, and the taurin, also, finds exit in the urine as an unoxidized sulphur compound, whilst the cholalic acid is discharged with the feces. All of this is changed in acute yellow atrophy. We owe to Frerichs the remarkable fact that the urea is greatly diminished, and sometimes entirely disappears from the urine in this disease. It is true there are some contradictory observations, but on the whole it seems clear that although urea may be present it is much less in amount than in the normal. Intermediate in the process of tissue metamorphosis are leucin and tyrosin, supposed to be steps in the transformation of albuminous substances into urea. We owe also to Frerichs the demonstration of the fact that these bodies appear in the urine, taking the place of urea. Tyrosin appears to be more frequently absent than leucin, which most observers agree is constantly present. Schultzen and Riess found, also, in the urine a peptone-like substance. These physiological chemists regard the presence of leucin and tyrosin in the urine as significant as albumen in Bright's disease, and sugar in diabetes. Prof. H. C. Wood, M.D., is disposed to the same view for leucin, and he would entitle the disease *leucinosis* (see the No. of this Journal for April 1867, p. 418), a term of which, we have seen, Dr. Legg especially disapproves. Thierfelder, speaking on this relation of leucin to urea, says: "We can hardly avoid tracing a connection between its appearance in the urine and the absence of the urea, and regarding a portion at least of the leucin as representative of the urea. That the actual production of the latter substance, and not merely its elimination from the blood, is interfered with, is extremely probable, because in other diseases in which the degeneration and functional derangement of the kidneys is quite as considerable as it is here, such a disappearance of the urea from the urine is not observed." (p. 288.) Dr. Legg expresses similar opinions, tinged in this case, we believe, with a judicious skepticism.

> "The disappearance of the urea from the urine together with the inorganic salts, taken together with the appearance of leucin and tyrosin, and, according to Schultzen and Riess, of a peptone, is a matter of the very deepest interest. In the present state of physiology, the place where the urea is formed is most uncertain, but the disappearance of urea from the urine leaves no room for surprise in a pathological state where every gland and every muscle is found acutely degenerated. It is interesting to observe the appearance of lower grades of tissue metamorphosis, such as leucin and tyrosin, in the urine, which some physiologists seem inclined to believe are early steps in the every-day change of albumen into urea."

As the liver has some office in connection with sanguification, and the maintenance of animal heat, it is important, from our present stand-point, to note the changes in the blood and in the temperature in this disease. As usual, there are contradictory statements, but we extract from the mass the fact that a diminution of the red and an increase of the white corpuscles take place; that the red corpuscles are changed in form; and that leucin, sometimes also tyrosin and urea, and cholesterine, are found. The hemorrhagic diathesis, which is a pronounced symptom, is not due, it is conceded generally, to the state of the blood, but to important alterations in the walls of the vessels.

In this as in other cases of jaundice, the temperature falls below normal, and remains so until the nervous phenomena develop. This decline in temperature means an arrest of those heat-producing processes in the liver which cause the blood of the hepatic vein to have a higher temperature than the blood of the portal. Furthermore, the glycogen, which we have seen is so widely distributed, so important to nutrition, and which serves to supply a readily available force by its oxidation, is no longer produced, at least, in any considerable quantity. Hence the failure of the liver to produce this material, affects heat-production throughout the organism. With the development of the nervous phenomena near the close of the case, some elevation of temperature occurs, and immediately after death a considerable elevation has taken place in some reported examples. It is uniformly observed that the temperature during the time when jaundice is developing is normal or considerably below normal, falling to 96° or 95.5° F. in some cases, before other elements besides the arrest of the hepatic function enter into the morbid complexus. Although the disturbance of the cerebral functions is usually accompanied by some febrile excitement, this is not always so, and Traube asserts that the condition of delirium does not affect the temperature.

The cerebral functions are disturbed to a greater or less extent after the jaundice has appeared, as a rule. The causes of this disturbance, from the point of view of the offices of the liver in the animal economy, are extremely important and instructive. Certain initiatory symptoms may give warning of the violent disturbance to follow; the patient may be suddenly seized with delirium and become insensible. Dr. Legg insists on the importance of dilatation of the pupil as the initial phenomenon, and the occurrence of which should excite apprehension in any case of jaundice. Thierfelder says that, besides being dilated, the movements of the pupil are sluggish. Rarely, rather, the pupils are contracted. Then come on a violent headache, restlessness, insomnia, or there may be stupor, indifference, prostration. Or "palpitation of the heart, with strongly accentuated first sound, abnormal sensitiveness to light and sounds, fainting," etc., may usher in the more formidable symptoms. Or, in still other cases, without any warning, delirium of a violent kind may ensue, or insensibility come on. Sometimes, in the midst of profound coma, an access of acute delirium may be manifest. The delirium varies in severity from a momentary incoherence up to the wildest mania. The coma manifests an equal variability: it may be a slight somnolence, or such depth of insensibility that no irritation can arouse. Convulsions also appear occasionally in adults—nearly if not quite constantly in children. These also vary from twitching of a few facial muscles up to a general epileptiform seizure, or a tetanic spasm. Legg finds that in 100 cases of the genuine disease, analyzed by himself, there were in 76 coma, in 59 delirium, and in 32 convulsions—results in general conformity to the usual observations.

In these cerebral effects, every one must be attracted by the resemblance to the symptomatology of certain poisons. The extraordinary likeness of acute yellow atrophy to phorphorus poisoning, already mentioned, will be hereafter discussed. Now the question pressing for answer is—What morbid products present in the blood can produce such disturbances? Are they of hepatic origin? We have already furnished the data for a decision on some points. The probability of the existence of the *cholesteræmia* invented by Dr. Flint, and developed by him with great ingenuity into a morbid state, must, in view of recent researches, be denied. The absorption of bile into the blood, which occurs in ordinary jaundice, is not accompanied by such symptoms. Leyden, it is true, affirms that the bile acids, which are known to act destructively on the red corpuscles when injected into the veins of dogs, do produce nervous symptoms analogous to those of acute atrophy, but he is not supported by many facts necessary to this theory. Leucin and tyrosin injected into the blood produce no symptoms. Frerichs suggests that a special poison may be produced by the disintegrating glandular substance, and that the nervous symptoms may result from its action on nervous matter. It need hardly be stated that there is absolutely no proof of the existence of such a poison; therefore, the search for a cause of hepatic origin, to account for the nervous symptoms, proves fruitless. Are the nervous phenomena due to uræmia? Although there is a general resemblance in the nervous disturbances belonging to acute yellow atrophy and to Bright's disease, respectively, when we come to the examination of particulars, wide differences are seen. Although the urine contains little or no urea, and but a small amount of albumen, and is otherwise altered in character, it has a maximum specific gravity, excretion of poisonous matters goes on, and hence the ordinary conditions producing uræmic intoxication are wanting. Rokitansky and Frerichs were much inclined to the uræmic theory, but the more recent investigations have apparently conclusively decided against it. Thierfelder sums up in a few words the main points:—

> "The kidneys fail to present in most cases, either as respects their function or their anatomical condition, such derangements as are found in those affections in whose train uræmia is most constantly developed; and as regards the diminution or disappearance of the urea in the urine, it is much more probable, as will be presently shown, that the formation of this substance and not its elimination from the blood is impeded."

Traube refers the nervous symptoms, not to cholæmia, but to inanition of the brain, which H. Weber supposes to be the cause of the delirium in pneumonia, and in fevers. Not only is the brain inadequately supplied with blood, but the blood is damaged; among other ways, by the action of the bile acids on the red corpuscles, and by the imperfect preparation in the intestine of the material of nutrition. Legg, rejecting all extraneous causes except the anæmia of the brain—or inanition—finds in the changes which occur in the cerebral vessels and tissues, as described by Steiner and Wunderlich, sufficient explanation of the nervous phenomena. (p. 455.)

Authorities are agreed as to the remarkable analogy between the symptoms and morbid anatomy of acute yellow atrophy and phosphorus poisoning, and some indeed maintain their identity, as has been stated. Dr. Legg sums up with great success the points of agreement and difference.

> "The temptation to look upon acute yellow atrophy as identical with phosphorus poisoning is certainly very great. The features of the two states bear the closest resemblance. Both are seen much more often in women than in men, and preserve much the same proportion; both are rare in childhood, common from puberty to about 35, and then again become rarer. The symptoms likewise are almost identical; a gastric catarrh followed by jaundice, during the course of which nervous symptoms and hemorrhages are seen, the end being in most cases fatal. The only clinical distinction which has been made, and in my opinion, not very successfully, lies in the state of the urine. Schultzen and Riess, as already stated, believe that in acute yellow atrophy, leucin and tyrosin are present in the urine; while in phosphorus poisoning these bodies are absent. Setting aside the cases

of phosphorus poisoning in which these bodies are said to have been found, but which show some uncertainty, I must own, I do not think the distinction will hold. It seems very improbable that if the same grave changes in nutrition take place in both states, such bodies as leucin and tyrosin should not be common to both. The morbid anatomy of both diseases has been warmly contested. The state of the kidneys, stomach, glands, and muscles is admitted to be identical in both; but the liver is said by some to be always enlarged in phosphorus poisoning, and to show no real fatty degeneration but a mere fatty infiltration. This again is denied to be true constantly. It is said with a good show of reason, that the size of the liver in both diseases depends on the length of time that the disease has lasted; that the liver is large if the disease end early, and small if the disease last long in both."

Such close correspondence in the action of a poison and the behaviour of a disease would indicate, that the latter is produced by an unknown poison. It remains for future investigation to determine the nature of the cause. It would, indeed, be surprising if some mysterious germs, micrococci, or bacteria had not been summoned from the regions of the unknown to make plain the origin of unexplained conditions. Klebs has, as is known to all the world, found a specific parasite for almost all diseases (Beiträge zur Kentniss der Micrococcen—*Archiv für experimentelle Pathologie und Pharmacologie*, Bandes i. ii. und iii.). Eppinger, supported by Klebs, has discovered in great numbers in the ducts of the liver the *Microsporon septicum.* It cannot be said, however, that this discovery has awakened any enthusiasm, or prepared the way for a final solution of the problem.

Dr. Legg, after concluding the subject of acute yellow atrophy, devotes a chapter to "Yellow Fever." Although in respect to symptomatology there are very obvious points of difference, yet it is almost impossible to distinguish between them in the *post-mortem* examination. He does justice to Dr. Alonzo Clark, who first pointed out the fatty degeneration of the liver, and who was followed by Dr. Bache. In the course of this chapter he differentiates between acute yellow atrophy and yellow fever, showing that some of the historical examples of the latter were probably cases of the former—a fact which indicates the close clinical correspondence of the two affections. There must, then, be a family affinity in the poison causing these diseases, and phosphorus. Beside the careful comparison at all points of phosphorus poisoning with acute yellow atrophy, Dr. Legg devotes a special chapter (the XXIVth) to the former. He shows that phosphorus has become a fashionable agent for suicidal purposes, and that "scarcely a week passes but some bodies are brought in for examination to the Pathological Institute at Berlin." The method most commonly employed in Germany, is to infuse the heads of about one hundred matches in coffee. Although the employment of this agent for suicide is not common in this country, accidents happen, with children, who may eat match heads.

But sufficient attention has been given to this department of the subject, and we, therefore, pass on to *icterus febrilis* (Chapter XXVI.)—that form of jaundice which accompanies pneumonia and certain febrile affections. Various explanations have been offered. The most satisfactory causes are two: obstruction to the bile-ducts by a plug of mucus, or by catarrhal swelling of the mucous membrane, and parenchymatous degeneration, which occurs in consequence of persistent high temperature. The jaundice which appears during the course of malarial fevers, and which Dr. Legg thinks is not frequent, is due to catarrh of the ducts and consequent obstruction. He is certainly in error in regarding malarial jaundice as uncommon. He does not allude to a form of malarial jaundice which comes on without any febrile disturbance, like the cases of spontaneous ague-cake. Any one who has had experience in the malarial diseases of the Mississippi Valley, will recall examples of both; a jaundice coming on without any apparent febrile movement, and disappearing rapidly under quinia, and a splenic enlargement arising in the same way. It is, of course, known that various functional derangements occur, in place of the febrile, in acute and chronic malarial poisoning: jaundice may be the succedaneum of periodical fever. It is true, nevertheless, that the jaundice occurring in the course of malarial toxæmia may be produced by the extension to the bile-ducts of a catarrhal process in the duodenum.

In his account of *icterus neonatorum*, Dr. Legg gives the statistics of Dr. Kehrer, who had 474 cases under examination. Of these, 5.3 per cent. were jaundiced on the first day, 62.9 per cent. on the second day, 124.1 on the third day, and after that but few. In one-third of these, the jaundice was over by five days, but in the greatest number, by six to ten days. There are various explanations of the causes of this jaundice. Billard offers a satisfactory solution of the problem, for those cases, at least, of which the skin only is coloured. These, he says, are due to changes in the circulation of the skin, the fading leaving behind a yellowish tinge, like the fading of a bruise. The explanation of Frerichs seems to be satisfactory in the cases of true jaundice. It has been pointed out already that jaundice may be due to lowering of the blood-pressure in the portal system. When the umbilical cord is ligated, the blood which passed into the portal vein from the umbilical, is suddenly cut off. Although in strong infants the balance of the circulation is quickly restored, in weakly infants, the lungs not thoroughly distended, the conditions are brought about for the flow of bile into the blood, instead of into the ducts. In other cases, as Virchow has pointed out, the jaundice is catarrhal. There are, also, quickly fatal cases from congenital narrowing or deficiency of the gall-ducts.

Our author also describes an *icterus menstrualis*, in which a monthly jaundice appears, instead of the normal menstrual flow. This is so rare as to be a pathological curiosity rather. The last chapter of the work is on bilious diseases, which we have already examined. He does not consider any other diseases of the liver than those having relation to the biliary function. Congestion, inflammation, sclerosis, suppuration, amyloid disease, cancer, parasites, etc., and the diseases of the biliary passages, he is silent in regard to. He may intend to follow this with another work, in which all other topics than those he has here discussed will receive adequate treatment; but he gives no information about his future purposes. This work, on the whole, is disappointing. It is able, and exhibits both learning and industry; but there is much repetition due to an imperfect arrangement of the topics discussed, and faulty digestion and assimilation of the vast material here accumulated. Dr. Legg not only shrewdly comments on the facts and opinions of others, but he has no little original knowledge of his own to offer. It is much to be desired that he complete the subject by another volume which shall embrace the topics not included in the present work. There are many interesting and important diseases of the liver requiring elucidation, and on which, we doubt not, he would cast a brilliant illumination. Meanwhile we may supplement our running comments on these diseases of the liver involving the biliary function, and in a future number submit some criticism of the modern opinions and practice in respect to the other hepatic diseases. Notwithstanding the rather gloomy view taken by Dr. Legg of the modern contributions to hepatic physiology and pathology, we believe that substantial progress is being made. Especially is progress making in the department of hepatic therapeutics. As the treatment of diseases can make sure advances only on sound acquisitions in physiological pathology, we may draw from the advance in hepatic therapeutics the just conclusion that our knowledge of the liver is really extending. R. B.

ART. XIV.—*The Principles and Practice of Surgery, being a Treatise on Surgical Diseases and Injuries.* By D. HAYES AGNEW, M.D., LL.D., Professor of Surgery in the Medical Department of the University of Pennsylvania. Profusely illustrated. Vol. II. 8vo. pp. 1066. Philadelphia: J. B. Lippincott & Co., 1881.

THE first volume of "Agnew's Surgery" was noticed in the number of this Journal for January, 1879, and we have now the pleasure of welcoming the second, in which the author has treated chiefly of *injuries and diseases of joints, of amputations, of injuries and diseases of the genito-urinary organs, and of affections of the spine and mouth.*

The first chapter (Chapter XI. of the complete work) is devoted to the consideration of dislocations in general and in particular. That complete luxation may, in enfeebled subjects, occur without laceration of the capsule is regarded as possible, though we are "not aware of the existence of any specimen which establishes the statement." Manipulation is recognized as an old method of reduction, systematized and its process formularized, however, only by modern surgeons.

Compound dislocations are advised to be treated antiseptically, the author here, as elsewhere, showing himself favourable to "Listerism"; and it is declared to be the "safest course to cut away the displaced ends of the articulating bones." The Astley Cooper limit of time proper for the reduction of old dislocations, it is thought, may be materially extended in these days of anæsthetics and of intelligent manipulations, the patient having been duly informed of the dangers attending the attempt at replacement, and subjected for some days to preliminary preparatory movements.

Under the head of "dislocation of the inferior maxillary bone," notice is taken of subluxation and "noisy movements," as also of "cramp of the jaw" from spasmodic contraction of the anterior belly of the digastric muscle, such spasm being "easily removed by friction with the finger over the rigid muscle". Replacement of dislocated vertebræ is directed to be made, if possible, in all cases.

Separation of the clavicle and the acromion process are denominated dislocations of the scapula, instead of the more usual "of the outer end of the clavicle;" and for the same reasons, the displacements at the ankle are described as luxations of the foot, instead of the bones of the leg. In the treatment of the various forms of clavicular and scapular luxations no mention is made of the use of plaster of Paris, which certainly best fulfils the one essential indication of securing as completely as possible the immobility of the replaced parts.